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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,568	KISHORE ET AL.	
	Examiner	Art Unit	
	SUSAN HANLEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-103* is/are pending in the application.

4a) Of the above claim(s) *3-5,15 and 30-103* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6-14 and 16-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, drawn to an erythropoietin production inducing peptide (EPIP), claims 2 and 6-29 (it is noted that claims 3, 4 ,5 and 103 which depends from claim 2 are drawn to a different invention, an EPIP and erythropoietin, which is properly grouped with Group I), and the species wherein R_1 and R_2 are H, X is O, L is polyalkylene and R_3 is hydroxy in the reply filed on 7/10/09 is acknowledged. The traversal is on the ground(s) that that there is no serious burden for the examiner to examine all of the inventions and species. This is not found persuasive because the restriction was based on 35 USC 371 in which the determination of restriction is based on lack of unity, or the lack of a common special technical feature between the groups. Lack of unity between the groups was demonstrated by the citation of WO 01/66149 which showed that the claims failed to make a contribution over the prior art and therefore failed to provide a special technical feature common to all of the claimed inventions. Regarding the species, lack of a common special technical feature was demonstrated because the various substitutions for the variables defines different compounds having distinct structures, chemical and physical properties. Hence, lack of unity was demonstrated.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-5, 15 and 30-103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. (It is noted that claim 5 depends from claim 104 and that there is no claim 104; it is assumed that this is a typographical error and that claim 5 depends from claim 103). Applicant

timely traversed the restriction (election) requirement in the reply filed on 7/10/2009. It is noted that new claim 103 depends from claim 2 which is drawn only to an EPIP. Claim 103 and its dependent claims are drawn to an EPIP and erythropoietin which is the invention of Group I which was not elected. Hence, the claims, even though they depend from claim 2 are properly withdrawn. Claim 15 is withdrawn because the structure of poly-D-glutamic acid does not read on the backbone of either elected specie for I or II. Therefore, it does not meet the structure of the elected specie.

Claims 2, 6-14 and 16-29 are presented for examination.

Specification

The abstract of the disclosure is objected to because it is too long. An abstract should range in length between 50 and 150 words. The instant abstract is about 170 words. Correction is required. See MPEP § 608.01(b).

The specification is objected to because in the Brief Description of the Drawings, there is no disclosure relating to all of the sub-figures included in a figure. Figures 21, 22 and 27 have multiple parts (21 a and b; 22 a and b; and 27 a-d). Each figure must be described.

Claim Rejections - 35 USC § 112

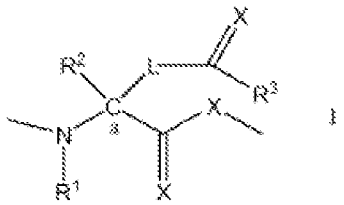
The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 6-12, 14 and 16-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 2 is generically drawn to a composition comprising an EPIP. The elected specie has a partial structure of formula I or II:



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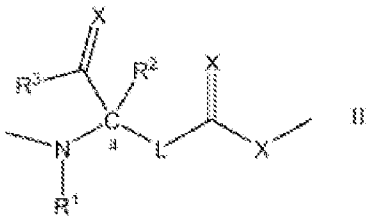


II

R_1 and R_2 are H, X is O, L is polyalkylene and R_3 is hydroxy. The EPIP comprises at least two residues of I or II and can have a tethered carboxylic acid group, a tethered amide group a tethered ester group or a salt thereof.

Neither structure I or II has sufficient description in the specification, nor are a representative number of compounds described within any one of these genera to demonstrate that applicant was in possession at the time of filing of any one of these genus terms.

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc.,

107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents" of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers,* 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe,* 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents" of the University of California v. Eli Lilly & Co.,* 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must

describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a

representative number of species to adequately describe a broad generic. In *Gostelli,* the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli,* 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for *a prima facie* case are discussed below.

In the instant case, the claims are drawn to a composition comprising an EPIP comprising at least two residues having the formula I or II.

(1) Level of skill and knowledge in the art:

The level of skill and knowledge in the art is high.

(2) Partial structure:

The specification teaches that the EPIP is a peptide comprising at least two residues having the formula I or II wherein the residues can be tethered. The specification fails to disclose any compounds having either the partial structure of I or II. The specification does not disclose any structures of a tethered compound having the structures I or II incorporated therein. Although the specification fails to disclose compounds having either partial structure I or II, one could envisage compounds having only residues of formula I, formula II or a mixture thereof. It is noted that the elected specie do not correspond to a peptide backbone, -NH-CHR-(C=O)-NH-CHR-(C=O)-.

(3) Physical and/or chemical properties and (4) Functional characteristics:

Applicant has not set forth the physical and/or chemical properties and functional characteristics for a composition comprising an EPIP having structures I or II. The specification fails to disclose the relationship between the partial structure and how the structural features of I or II induce the proliferation and differentiation of cells that synthesize erythropoietin. The specification appears to be devoted instead to the induction of cells that produce erythropoietin by poly-D-glutamic acid. Poly-D-glutamic acid does not have the formula I or II in its structure.

(5) Method of making the claimed invention:

The specification fails to teach how to make any compounds having the formulas I or II.

As stated *supra,* the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that the claims are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations of compounds having formula I or formula II as they read on the elected specie are limitless. Although the claims may recite some functional characteristics (e.g. that the EPIP induces the production of erythropoietin), the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds that comprise formulas I or II as they read on the elected specie. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description for EPIPs that comprise only residues having formula I, formula II or a mixture thereof (since such compounds are easily envisaged), the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims. Because the claims encompass a multitude of compounds neither contemplated nor disclosed by the as-filed disclosure, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder,* 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 2, 6-14 and 16-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright,* 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]
>
> [1]As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands',* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman,* 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

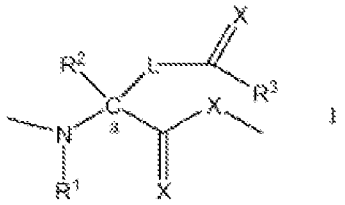
1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,

3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of those in the art,
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108,427 F.2d 833,839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands" factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to a composition comprising an EPIP that comprises at least two residues having the formula I or II:



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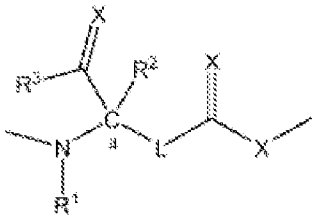

II

wherein the elected species is directed to a structure wherein R_1 and R_2 are H, X is O, L is polyalkylene and R_3 is hydroxy. The EPIP can have a tethered carboxylic acid group, a tethered amide group a tethered ester group or a salt thereof.

The relative skill of those in the art is high, generally that of a PhD biochemist and a PhD organic chemist.

That factor is outweighed however by the unpredictable nature of the arts of biochemistry and organic synthesis.

The proliferation and differentiation of cells and what induces them to proliferate is complex and not well understood. Cells comprise a multitude of complex molecules (DNA, RNA, proteins etc.) and structures (nucleus, receptors, membranes, etc.). The interaction of a compound could be with any of these entities to stimulate cell production. Mann et al. (US 5,919,464) disclose that research on agents that are potentially useful for regulating or modulating cellular activity in vitro or in vivo has "identified compounds erratically effective in affecting the differentiation and/or the proliferation of a very narrow range of cell types under carefully controlled conditions". Mann et al. state that such research has been of limited focus due to the complexity of the "poorly-understood pathways by which cellular proliferation and differentiation are regulated, the unpredictalbe point at which these prior art compounds intervene in these pathways, and the consequently substantially random nature of the effects of these compounds on the basic underlying mechanisms controlling differentiation and proliferation" (col. 3, lines 47-60). Therefore, the prior art recognizes the unpredictability of determining agents that will induce cellular proliferation and/or differentiation. Hence, there is

no way for one of skill in the art to know, a priori, if a given compound can induce cell proliferation in order to produce a particular protein.

Organic chemistry involves the reaction of chemical entities to make desired products. However, the art is unpredictalbe due to unknown factors that can influence a chemical reaction. That is, one must consider the chemical and physical properties of the reactants and products, the reaction conditions and the desired course of the reaction. Any of these factors can have unknown or hidden aspects that will confound the predicted course of a reaction. There is no way for one skill in the art to know, a priori, if a given an unknown chemical reaction will proceed to the desired reaction products with a reasonable expectation of results.

Thus, the state of the prior art does not support the broad scope of the above claims.

2. The breadth of the claims

The claims are broad insofar as they disclose an EPIP having at least two residues of structure I or II as the structures read on the elected species.

3. The amount of direction or guidance provided and the presence or absence of working examples

Regarding the induction of cellular proliferation to produce erythropoietin, the specification teaches the production of erythropoietin depends upon the induction of the proliferation of peritubular fibroblast-like cells (PTFBLC; specification page 14, lines 15-17). The specification teaches that the induction effect of PTFBLC can be direct or indirect. There is no disclosure related to what direct induction entails. Indirect induction results from the effect of a compound on other cells. Compounds can stimulate proximal tubular cells to release certain molecules (that are not disclosed by the instant specification) that stimulate erythropoietin-

producing PTFBLC. The specification teaches that the disclosed compounds affect a lysosomal storage condition in the proximal tubular cells that somehow stimulates the proliferation of PTFBLC (specification page 15, lines 9-16). The specification discloses the effect of poly-D-glutamic acid on proximal tubular cells and teaches that poly-D-glutamic acid stimulates peritubular cells in the rat kidney (specification pages 69-70). The specification does not teach what structural features of poly-D-glutamic acid causes these effects. The specification does not teach the administration of any compounds having the structures I or I as they read on the elected specie thereof, to any type of cells to induce cells to proliferate and to produce erythropoietin. The specification does not teach what structural features of compounds having the formula I or II may effect proliferation of any cells that produce erythropoietin.

Regarding the synthesis of compounds having at least two residues having formula I or II as they read on the elected specie, the specification does not disclose any compounds having said formula in their structures. The specification discloses how to make peptide bonds (pages 21-22 of the specification) but fails to teach how one makes a compound that incorporates the backbone N-C-C-O (formula I) or N-C-C-C-O (formula II) into any compound whether it comprises only formula I, formula II or a mixture thereof (instant claim 13) or a compound that comprises at least two residues of either formula I or formula II. Regarding compounds that contain only the structures of formula I and II as they read on the elected species, the specification does not teach how to make a compound having the backbone N-C-C-O-N-C-C-O (only formula I), N-C-C-C-O-N-C-C-C-O (only formula II), or a mixture thereof. It is noted that said backbones are not peptides and the specification does not teach how to make compounds with such backbones.

4. The quantity of experimentation necessary

Because of the known unpredictability of the biochemical art regarding the induction of cellular proliferation (as discussed supra) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that any compounds containing at least two residues of the elected species of formula I or II could predictably induce the proliferation of cells that produce erythropoietin as inferred in the claims and contemplated by the specification.

Because of the known unpredictability of the chemical arts regarding the synthesis of organic compounds (as discussed supra) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that one could predictably synthesize compounds having at least two residues of the elected specie of formula I or II in a compound inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

To practice the invention of the instant claims requires undue experimentation due to unpredictability of the induction of cellular proliferation and the lack of direction from Applicants regarding the same. The amount of experimentation required in order to induce the proliferation of cells that produce erythropoietin by compounds of the elected species containing at least two residues of formula I or II is extremely large and the methodology of inducing

cellular proliferation by compounds containing the formula of the elected specie would require inventive effort and extensive experimental burden.

To practice the invention of the instant claims requires undue experimentation due to the unpredictability in the formation of compounds having at least two residues of formula I or II as pertaining the elected specie therein and the lack of direction from Applicants regarding procedures for the formation of the same. The amount of experimentation required in order to produce compounds having at least two residues of formula I or II as pertaining the elected specie therein is extremely large and the methodology of production of the claimed compounds would required inventive effort and extensive experimental burden.

In light of the above discussion, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susan Hanley/
Examiner, Art Unit 1651

/Irene Marx/
Primary Examiner
Art Unit 1651